REMARKS

A. Interview with the Examiner

Applicants thank the Examiner for the courtesy extended to Applicants' representatives during a telephonic interview held on January 3, 2007. During the interview, Applicants discussed the rejections under 35 U.S.C. §§ 112 and 103(a). Applicants emphasized that the proposed combination of references for the rejection of Applicants' claims under 35 U.S.C. § 103(a) was improper, because one of the references (Riordan) actually taught away from combination proposed by the Examiner. These arguments are reiterated and expanded upon below.

B. Information Disclosure Statement

In the Office Action issued on October 30, 2006, the Examiner indicated that she had considered all of the references that had been previously cited by Applicants, with the exception of the "Nakamura et al." reference. Because the Examiner indicated that she had not received a copy of this reference, Applicants have submitted with this response another Information Disclosure Statement, including a PTO-1449 form and a copy of the Nakamura reference for the Examiner's review. Applicants also include U.S. Patent No. 5,792,449 for consideration by the Examiner.

C. Status of the Claims and Explanation of the Amendments

1. Claims Under Examination

Currently, claims 1-114 are pending. Claims 2-23, 30, 31, 36-67, 73, 76-98, and 111-112 have been withdrawn by the Examiner. In this response, Applicants have requested the cancellation of claims 29, 32, 68-72, 101, 104, 110 without prejudice or disclaimer. Applicants hereby reserve the right to pursue the cancelled subject matter in subsequent continuation applications.

Additionally claims 115-125 have been added. Support for these new claims is generally found in the specification [e.g., see Example 1 and paragraphs [29] and [39]].

When these claim cancellations and new claims have been entered, the claims presented for examination will be claims 1, 24-28, 33-35, 99, 105-109, and 111-125.

2. Claim Rejections

Claims 1, 24-29, 32-35, 68-72, 74-75, 99-110, and 113-114 have been rejected under 35 U.S.C. § 112, ¶1, for allegedly failing to comply with the written description requirement.

Claims 68-72, 74-75, and 102-104 remain rejected under 35 U.S.C. § 112 ,¶ 2 for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claims 1, 24-29, 32-35, 68-72, 74-75, 99-110, and 113-114 have been rejected under 35 U.S.C. § 103(a) for allegedly being unpatentably over U.S. Patent No. 6,573,299 to

Petrus ("Petrus"), in view of U.S. Patent No. 5,866,142 to Riordan ("Riordan"), and in further view of U.S. Patent No. 6,113,636 to Ogle ("Ogle").

3. Claim Amendments

Claims 1, 24, and 105 have been amended to clarify the invention and now each claim recites a Markush group. Support for these amendments is found in original claim 5, as well as paragraph [29] of the original specification.

Claims 27 and 28 have been amended to recite "wherein the composition is zinc citrate" and "wherein the composition is zinc carbonate", respectively. Support for these amendments are found in paragraph [29] of the specification. In amending claim 28, Applicants are mindful that Applicants previously made a species election of "zinc citrate" in Applicants' response to the election/restriction requirement issued by the Examiner on December 6, 2005. However, Applicants respectfully note that 37 C.F.R. § 1.141 specifically allows for the claiming of more than one species of an invention, and accordingly Applicants request examination of zinc carbonate as a species embraced by the invention, particularly in view of claim 1 being a linking claim.

Additionally, Applicants respectfully note that the zinc-containing species recited in the Markush groups of new claims 118 and 122 are mutually exclusive of those species recited in Petrus (e.g., see Petrus, col. 13, lines 16-29). For at least this reason, Applicants respectfully assert that claims 118 and 122 (and corresponding dependent claims) are patentable over Petrus.

C. Response to the Rejections Under 35 U.S.C. §112.

1. The Rejection Under 35 U.S.C. §112, ¶1.

Claims 1, 24-29, 32-35, 68-72, 74-75, 99-110, and 113-114 are rejected because the Examiner contends that there is no written description in the specification to support the recitation of "zinc pyrithione" in those claims. In view of the amendments to independent claims 1, 24, and 105 set forth in this paper, this rejection is moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

2. The Rejection Under 35 U.S.C. §112, ¶2

The Examiner maintains the rejection of claims 68-72, 74-75, and 102-104, alleging that the phrase "in the vicinity of the lens" is indefinite, for the reasons set forth in the previous Office Action dated February 15, 2006. To expedite prosecution, Applicants have requested the cancellation of claims 68-72, 74-75, and 102-104. The request for cancellation of these claims is made without prejudice or disclaimer of Applicants' rights to file and to prosecute claims directed to the cancelled subject matter in a continuation application claiming priority to this application.. Accordingly, the rejection of these claims under 35 U.S.C. § 112, ¶ 2 is now moot.

D. Response to the Rejections Under 35 U.S.C. §103(a)

Applicants respectfully traverse the rejection of claims 1, 24-29, 32-35, 68-72, 74-75, and 99-104 under 35 U.S.C. §103(a) for allegedly being unpatentable over Petrus, in view of Riordan and Ogle. As Applicants noted in the previous response and during the telephonic

interview of January 3, 2007, Riordan teaches away from the combination of references proposed by the Examiner. Accordingly, the rejection should be withdrawn. See MPEP § 2145.

1. Riordan Teaches Away from the Proposed Combination

Previously, the Examiner noted that Petrus indicates that zinc may be applied topically [see page 11 of the Office Action of February 16, 2006, citing Petrus, at col. 13, lines 21-28]. However, the Examiner conceded that "Petrus does not expressly teach that topical application of the disclosed active composition increases elastin content in the tissue." [Office Action of February 16, 2006, at page 12]. To alleviate this deficiency, the Examiner relied upon Riordan for its discussion of the role of elastin breakdown in aging skin [see page 12 of the Office Action of February 16, 2006, citing Riordan, col. 2, lines 18-34]. A rejection based on this combination of references has been maintained in the Office Action of October 30, 2006.

Applicants respectfully submit that this reliance upon Riordan in both Office Actions is misplaced, because Riordan actually teaches away from the proposed combination for at least the following reasons:

(1) **Riordan states that the presence of mineral salts in the folds of elastin molecules of the skin is one of the causes of aging skin.** According to Riordan, the presence of mineral salts in the folds of elastin molecules leads to increased rigidity of the elastin molecules in the skin and an appearance of aging. Specifically, Riordan states the following:

> As described above, the aging human skin is characterized in part by a loss in elasticity which is attributed to the attraction of mineral salts, particularly calcium salts, by lipids deposited in the protein folds of elastin

> molecules, increasing the rigidity of, and solidifying the aging elastin molecules. (Riordan, col. 4, lines 38-43, emphasis added).

While Riordan's specification states that calcium salts are particularly deleterious, the discussion of "mineral salts" in Riordan's specification is not specifically limited to calcium salts, and includes other mineral salts containing divalent cations.

(2) **Riordan states that divalent cations should be removed.** Consistent with Riordan's identification of the deleterious effect of calcium and other divalent cations on elastin, Riordan not only teaches away from adding mineral salts to skin, but specifically teaches the removal of divalent cations that are already in the skin by the addition of divalent cation chelators. According to Riordan,

> [t]he molecule histidine, and other divalent cation chelators, are able to remove when applied topically to the skin of human beings, mineral salts, in particular, the mineral calcium [Riordan, col. 4, lines 43-46]..

Thus, while Applicants' claim the administration of zinc (e.g., which can be a divalent cation, Zn^{+2}, see specification, paragraph 17) to aging skin to enhance the growth of elastin, Riordan teaches the ***removal*** of divalent cations (which would include removing Zn^{+2}) from the skin by isolating them with divalent cation chelators.

In summary, neither Petrus or Riordan, alone or in combination, teach or suggest the addition of zinc to increase the elastin content in aging skin. Moreover, while Petrus urges the topical application of zinc to inhibit nitric oxide synthase [*see* Petrus, col. 13, lines 16-29], Riordan teaches against topical application of zinc by (1) warning that mineral salts (which would include zinc salts) in aging skin adversely affect the elasticity of the skin, and (2) stating

that divalent cations of those mineral salts (which would include Zn^{+2}) should be removed from aging skin. Accordingly, Riordan teaches away from the Examiner's proposed combination of Petrus and Riordan.

Ogle does not alleviate the deficiencies in the proposed combination of Petrus and Riordan, because Ogle only refers to the use of zinc for antimicrobial purposes, not for increasing elastin [see, e.g., Ogle, col. 4, lines 18-20]. Thus, Ogle would not teach, disclose or suggest to one of ordinary skill in the art to apply zinc to skin in need of additional elastin (e.g., aging skin) to arrive at the invention recited in Applicants' claims.

2. The Examiner Applies the Wrong Standard and Misinterprets *In re Keller*

In Applicants' previous response, Applicants had also noted that Riordan taught away from the Examiner's proposed combination. In response, the Examiner alleges that Applicants were impermissibly "attempting to bodily incorporate the teachings of Riordan into the teachings of the primary reference without considering the context in which Riordan was cited and the teachings gleaned from the reference and relied upon for the basis of the rejection" [Office Action, page 11, citing *In re Keller* 642 F. 2d 413, 1981 CCPA LEXIS 262, 208 U.S.P.Q. (BNA) 871].

Applicants respectfully disagree with the Examiner's reliance on *In re Keller*. As stated in § 2141.02 of the MPEP, "the prior art must be considered in its entirety, including disclosures that teach away from the claims" (emphasis added). Thus, the Examiner's attempt to limit the scope of the discussion of Riordan to only "the context in which Riordan was cited" is improper and inconsistent with the guidelines set forth in the MPEP.

Moreover, the Examiner's reliance upon *In re Keller* is unavailing, because the cited portion of this case actually supports Applicants' position, not the Examiner's. According to *In re Keller*,

> [t]he test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to one of ordinary skill in the art. [*In re Keller*, 642 F. 2d 413, 425 (emphasis added)].

Thus, *In re Keller* makes it clear that one should consider the "***combined*** teachings of the references", which must include any portion of a reference that teaches away from the proposed combination, if one truly considers the "***combined*** teachings". To selectively focus on Riordan's discussion of elastin breakdown, without also considering Riordan's express warnings to avoid adding mineral salts to aging skin or to remove divalent cations in aging skin because such divalent cations have deleterious effects on the skin (as the previous two Office Actions had failed to do), would violate the requirement of *In re Keller* to consider the "combined teachings of the references".

3. The Concentration of Zinc is Not Simply a "Result-Effective Variable" As Alleged by the Examiner

The Examiner contends that that it would be routine to determine the optimum concentration of zinc, and thus suggests that Applicants' claimed zinc concentration range (e.g., as recited in claim 105) is obvious over Petrus. Specifically, the Examiner states that

> the concentration of zinc is a result-effective variable, i.e., a variable that achieves a recognized result, and therefore, the determination of the optimum of workable dosage range would be well within the practice of routine experimentation by the skilled artisan, absent factual evidence to the contrary, and further, absent any evidence demonstrating a patentable difference between the compositions used and the criticality of the amounts [Office Action of October 30, 2006, p. 8].

Applicants respectfully disagree. As shown in Example 1 of Applicants' specification, even though elastin is formed when a "high" zinc concentration is used, elastin formation is accompanied by irritation and sloughing. Thus, to assert that the zinc concentration is merely a "variable that achieves a recognized result" overlooks the significance of Applicants' claimed range, as exemplified in Example 1 of Applicants' specification. This is further illustrated in Example 9 of Applicants' specification, which shows that elastase, a naturally occurring enzyme in the human body that causes the breakdown of elastin, can be inhibited when the zinc concentration is in a certain range. Unlike most dose-response curves, which reach a plateau, when the zinc concentration is either above or below the appropriate range, the breakdown of elastin by elastase actually increases. Thus, the Examiner's characterization of zinc as "a variable that achieves a recognized result" is improper, because none of the references of record recognize that high amounts of zinc can lead to irritation and sloughing, as well as undesirable increased elastase activity. Similarly, none of the references of record recognize that very low amounts of zinc can lead to undesirable increased elastase activity, as taught in Applicants' specification (e.g., Example 9).

Furthermore, Petrus does not teach or suggest the "about 1.0 pM to about 10 mM" zinc concentration ranges recited in Applicants' claims. In fact, Petrus is silent on zinc

concentrations, with the exception of Examples 1 and 2, which mention compositions containing 2% zinc lineolate. However, a 2% zinc lineolate composition corresponds to a zinc lineolate concentration of 58 mM, which is outside Applicants' claimed range of "about 1.0 pM to about 10 mM", as the following calculations show:

$$2\,\%\ \text{zinc lineolate} = \frac{2\ \text{grams of zinc lineolate}}{100\ \text{ml of composition}} \qquad (1)$$

$$\frac{2\ \text{grams of zinc lineolate}}{100\ \text{ml of composition}} \times \frac{1\ \text{mol}}{344\ \text{g}} \times \frac{1000\ \text{ml}}{1\ \text{liter}} = 0.058\ \text{M} = 58\ \text{mM} \qquad (2)$$

Moreover, Petrus states that "[t]he suggested topical dose range of the present invention is 10 to 20 mg per day" [Petrus, col. 13, lines 19-21]. In contrast, the zinc dosage ranges contemplated by Applicants are lower than the 10 - 20 mg daily range described by Petrus. Consider, for example, Applicants' inventive topical composition containing zinc citrate, the zinc-containing species that has been elected for examination. The following calculation shows that if one were to apply 0.2 ml of a 10 mM zinc citrate composition, the total zinc citrate dose would only be 1.22 mg, nearly an order of magnitude less than the low end of Petrus's recited range:

For these calculations, it is assumed that 0.2 ml of the composition is applied, a volume that approximates a dab of lotion around the eye (see also Example 1 of Applicants' specification).

$$0.2\,\text{ml of composition} \times \frac{10\,\text{millimoles zinc citrate}}{1000\,\text{ml of composition}} = 0.002\,\text{millimoles zinc citrate} \quad (3)$$

$$0.002\,\text{millimoles zinc citrate} \times \frac{1\,\text{mole}}{1000\,\text{millimoles}} \times \frac{610.37\,\text{grams zinc citrate}}{1\,\text{mole}} = 0.0012\,\text{grams} \quad (4)$$

$$= 1.2\,\text{mg of zinc citrate.}$$

Similar calculations for the other zinc compounds that are recited in both Petrus and Applicants' claims under examination reveal that the total zinc dosages of these compounds, assuming an applied volume of 0.2 ml, are also less than the 10 - 20 mg range recited in Petrus.

Based on the foregoing, Applicants' claims are patentable over Petrus, in view of Riordan and Ogle. Reconsideration and withdrawal of the rejections of Applicants' claims are respectfully requested.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-3732**, Order No. 103720-105089US1. In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-3732,** Order No. 103720-105089US1.

Respectfully submitted,
KING & SPALDING, L.L.P.

Dated: March 30, 2007

By: _____
Joseph D. Eng Jr. / Kenneth H. Sonnenfeld
Reg. No. 54,084 / 33,285

Correspondence Address:
King & Spalding, LLP
(212) 827 - 4318 Telephone
(212) 556 -2222Facsimile